

09756690 .041902

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Kolterman, et al.

Serial No.: 09/756,690

Filed: January 9, 2001

Title: USE OF EXENDINS AND AGONISTS  
THEREOF FOR MODULATION OF  
TRIGLYCERIDE LEVELS AND  
TREATMENT OF DYSLIPIDEMIA

Group Art Unit: 1614

Examiner: To be assigned

TECH CENTER 1600/2900

APR 24 2002

RECEIVED

Commissioner of Patents and Trademarks  
Box Sequence, P.O. Box 2327  
Arlington, VA 22202

Dear Sir:

**PRELIMINARY AMENDMENT**

In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed December 13, 2001, Applicants submit herewith a corrected sequence listing and further request that the following amendments to the specification be entered.

In the Specification

(a) On page 15 of the specification as filed, please amend the first full paragraph under "BRIEF DESCRIPTION OF THE DRAWINGS" to read:

--Figure 1 depicts the amino acid sequences for certain exendin agonist compounds useful in the present invention [SEQ ID NOS 9-39] (peptide listed above the table is SEQ ID NO: 3).—

CERTIFICATE OF MAILING  
(37 C.F.R. §1.8a)

I hereby certify that this paper (along with anything referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage in an envelope addressed to the Commissioner for Patents, Patent and Trademark Office, Box Sequence, P O Box 2327, Arlington, VA 22202

April 15, 2002  
Date of Deposit

Amanda Halverson  
Name of Person Mailing Paper  
Amanda Halverson  
Signature of Person Mailing Paper

(b) On page 24, second full paragraph, through page 27, up to but not including “Definitions,” please amend the paragraph and formula (III) [SEQ ID NO. 5] as follows:

--Exendin agonist compounds also include those described in International Patent Application No. PCT/US98/24273, filed November 13, 1998, entitled, “Novel Exendin Agonist Compounds,” which claims the benefit of United States Provisional Application No. 60/066,029, filed November 14, 1997, including compounds of the formula (III) [SEQ ID NO. 5]:

Xaa<sub>1</sub> Xaa<sub>2</sub> Xaa<sub>3</sub> Xaa<sub>4</sub> Xaa<sub>5</sub> Xaa<sub>6</sub> Xaa<sub>7</sub> Xaa<sub>8</sub> Xaa<sub>9</sub> Xaa<sub>10</sub>  
Xaa<sub>11</sub> Xaa<sub>12</sub> Xaa<sub>13</sub> Xaa<sub>14</sub> Xaa<sub>15</sub> Xaa<sub>16</sub> Xaa<sub>17</sub> Ala Xaa<sub>19</sub> Xaa<sub>20</sub>  
Xaa<sub>21</sub> Xaa<sub>22</sub> Xaa<sub>23</sub> Xaa<sub>24</sub> Xaa<sub>25</sub> Xaa<sub>26</sub> Xaa<sub>27</sub> Xaa<sub>28</sub>-Z<sub>1</sub>; wherein

Xaa<sub>1</sub> is His, Arg, Tyr, Ala, Norval, Val or Norleu;

Xaa<sub>2</sub> is Ser, Gly, Ala or Thr;

Xaa<sub>3</sub> is Ala, Asp or Glu;

Xaa<sub>4</sub> is Ala, Norval, Val, Norleu or Gly;

Xaa<sub>5</sub> is Ala or Thr;

Xaa<sub>6</sub> is Phe, Tyr or naphthylalanine;

Xaa<sub>7</sub> is Thr or Ser;

Xaa<sub>8</sub> is Ala, Ser or Thr;

Xaa<sub>9</sub> is Ala, Norval, Val, Norleu, Asp or Glu;

Xaa<sub>10</sub> is Ala, Leu, Ile, Val, pentylglycine or Met;

Xaa<sub>11</sub> is Ala or Ser;

Xaa<sub>12</sub> is Ala or Lys;

Xaa<sub>13</sub> is Ala or Gln;

Xaa<sub>14</sub> is Ala, Leu, Ile, pentylglycine, Val or Met;

Xaa<sub>15</sub> is Ala or Glu;

Xaa<sub>16</sub> is Ala or Glu;

Xaa<sub>17</sub> is Ala or Glu;

Xaa<sub>19</sub> is Ala or Val;

Xaa<sub>20</sub> is Ala or Arg;

Xaa<sub>21</sub> is Ala or Leu;

Xaa<sub>22</sub> is Phe, Tyr or naphthylalanine;

Xaa<sub>23</sub> is Ile, Val, Leu, pentylglycine, tert-butylglycine or Met;

Xaa<sub>24</sub> is Ala, Glu or Asp;

Xaa<sub>25</sub> is Ala, Trp, Phe, Tyr or naphthylalanine;

Xaa<sub>26</sub> is Ala or Leu;

Xaa<sub>27</sub> is Ala or Lys;

Xaa<sub>28</sub> is Ala or Asn;

Z<sub>1</sub> is -OH,

-NH<sub>2</sub>,

Gly-Z<sub>2</sub>,

Gly Gly-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub>-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser Gly-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub>-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub> Xaa<sub>37</sub>-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub> Xaa<sub>37</sub> Xaa<sub>38</sub>-Z<sub>2</sub> or

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub> Xaa<sub>37</sub> Xaa<sub>38</sub> Ser-Z<sub>2</sub>;

wherein Xaa<sub>31</sub>, Xaa<sub>36</sub>, Xaa<sub>37</sub> and Xaa<sub>38</sub> are independently

Pro, homoproline, 3Hyp, 4Hyp, thioproline, N-alkylglycine, N-alkylpentylglycine or N-alkylalanine; and

Z<sub>2</sub> is -OH or -NH<sub>2</sub>;

provided that no more than three of Xaa<sub>3</sub>, Xaa<sub>4</sub>, Xaa<sub>5</sub>, Xaa<sub>6</sub>, Xaa<sub>8</sub>, Xaa<sub>9</sub>, Xaa<sub>10</sub>, Xaa<sub>11</sub>,

Xaa<sub>12</sub>, Xaa<sub>13</sub>, Xaa<sub>14</sub>, Xaa<sub>15</sub>, Xaa<sub>16</sub>, Xaa<sub>17</sub>, Xaa<sub>19</sub>, Xaa<sub>20</sub>, Xaa<sub>21</sub>, Xaa<sub>24</sub>, Xaa<sub>25</sub>, Xaa<sub>26</sub>, Xaa<sub>27</sub>

and Xaa<sub>28</sub> are Ala; and provided also that, if Xaa<sub>1</sub> is His, Arg or Tyr, then at least one of Xaa<sub>3</sub>, Xaa<sub>4</sub> and Xaa<sub>9</sub> is Ala.--

### REMARKS

A marked up version of the amended paragraphs to show changes made is attached hereto. Additions are noted by underlining, deletions are noted by bracketing, and all changes have been bolded for convenient reference. The amendments are made not for reasons related to patentability, but to improve the readability of the specification and correct typographical errors. These amendments add no new matter.

The amendments to the specification find full support in the specification and in materials incorporated by reference. The amendment to the description of Figure 1 merely identifies the SEQ ID NO of the genus in the top portion of the Figure. That SEQ ID NO (SEQ ID NO 3) is further defined in the specification at page 17.

The amendment to Formula III identifies the residue Xaa<sub>39</sub> as Serine. This amendment is supported in the cited reference, PCT/US98/24273, duly incorporated by reference into the instant specification, by a genus in that specification within Formula III. The serine residue incorporated at position 39 is recited throughout the PCT/US98/24273 specification, for example on pages 9 and 23. These amendments therefore add no new matter and their entry is respectfully requested.

Patent

Atty. Docket: 030639.0066.UTL

Atty. Docket No.: 249/124 US

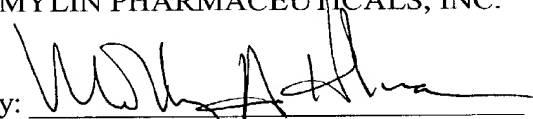
Applicant also requests that the Examiner enter the amended sequence listing, which is provided in both paper and computer readable form (diskette). The matter contained on the paper and diskette are identical, and add no new matter to the specification.

Date: April 15, 2002

Respectfully submitted,

AMYLIN PHARMACEUTICALS, INC.

By:



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**MARKED UP VERSION SHOWING CHANGES MADE**

Amendments to the referenced paragraphs are indicated by bold and underlining for additions and bolded brackets for deletions.

(a) On page 15, first full paragraph under "BRIEF DESCRIPTION OF THE DRAWINGS":

Figure 1 depicts the amino acid sequences for certain exendin agonist compounds useful in the present invention [SEQ ID NOS 9-39] **(peptide listed above the table is SEQ ID NO: 3).**

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Xaa<sub>1</sub> Xaa<sub>2</sub> Xaa<sub>3</sub> Xaa<sub>4</sub> Xaa<sub>5</sub> Xaa<sub>6</sub> Xaa<sub>7</sub> Xaa<sub>8</sub> Xaa<sub>9</sub> Xaa<sub>10</sub>  
 Xaa<sub>11</sub> Xaa<sub>12</sub> Xaa<sub>13</sub> Xaa<sub>14</sub> Xaa<sub>15</sub> Xaa<sub>16</sub> Xaa<sub>17</sub> Ala Xaa<sub>19</sub> Xaa<sub>20</sub>  
 Xaa<sub>21</sub> Xaa<sub>22</sub> Xaa<sub>23</sub> Xaa<sub>24</sub> Xaa<sub>25</sub> Xaa<sub>26</sub> Xaa<sub>27</sub> Xaa<sub>28</sub>-Z<sub>1</sub>; wherein

Xaa<sub>1</sub> is His, Arg, Tyr, Ala, Norval, Val or Norleu;

Xaa<sub>2</sub> is Ser, Gly, Ala or Thr;

Xaa<sub>3</sub> is Ala, Asp or Glu;

Xaa<sub>4</sub> is Ala, Norval, Val, Norleu or Gly;

Xaa<sub>5</sub> is Ala or Thr;

Xaa<sub>6</sub> is Phe, Tyr or naphthylalanine;

Xaa<sub>7</sub> is Thr or Ser;

Xaa<sub>8</sub> is Ala, Ser or Thr;  
Xaa<sub>9</sub> is Ala, Norval, Val, Norleu, Asp or Glu;  
Xaa<sub>10</sub> is Ala, Leu, Ile, Val, pentylglycine or Met;  
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Xaa<sub>12</sub> is Ala or Lys;  
Xaa<sub>13</sub> is Ala or Gln;  
Xaa<sub>14</sub> is Ala, Leu, Ile, pentylglycine, Val or Met;  
Xaa<sub>15</sub> is Ala or Glu;  
Xaa<sub>16</sub> is Ala or Glu;  
Xaa<sub>17</sub> is Ala or Glu;  
Xaa<sub>19</sub> is Ala or Val;  
Xaa<sub>20</sub> is Ala or Arg;  
Xaa<sub>21</sub> is Ala or Leu;  
Xaa<sub>22</sub> is Phe, Tyr or naphthylalanine;  
Xaa<sub>23</sub> is Ile, Val, Leu, pentylglycine, tert-butylglycine or Met;  
Xaa<sub>24</sub> is Ala, Glu or Asp;  
Xaa<sub>25</sub> is Ala, Trp, Phe, Tyr or naphthylalanine;  
Xaa<sub>26</sub> is Ala or Leu;  
Xaa<sub>27</sub> is Ala or Lys;  
Xaa<sub>28</sub> is Ala or Asn;  
Z<sub>1</sub> is -OH,  
-NH<sub>2</sub>,  
Gly-Z<sub>2</sub>,  
Gly Gly-Z<sub>2</sub>,  
Gly Gly Xaa<sub>31</sub>-Z<sub>2</sub>,  
Gly Gly Xaa<sub>31</sub> Ser-Z<sub>2</sub>,  
Gly Gly Xaa<sub>31</sub> Ser Ser-Z<sub>2</sub>,  
Gly Gly Xaa<sub>31</sub> Ser Ser Gly-Z<sub>2</sub>,  
Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala-Z<sub>2</sub>,  
Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub>-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub> Xaa<sub>37</sub>-Z<sub>2</sub>,

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub> Xaa<sub>37</sub> Xaa<sub>38</sub>-Z<sub>2</sub> or

Gly Gly Xaa<sub>31</sub> Ser Ser Gly Ala Xaa<sub>36</sub> Xaa<sub>37</sub> Xaa<sub>38</sub> [**Xaa<sub>39</sub>**] Ser-Z<sub>2</sub>;

wherein Xaa<sub>31</sub>, Xaa<sub>36</sub>, Xaa<sub>37</sub> and Xaa<sub>38</sub> are independently

Pro, homoproline, 3Hyp, 4Hyp, thioproline, N-alkylglycine, N-alkylpentylglycine  
or N-alkylalanine; and

Z<sub>2</sub> is -OH or -NH<sub>2</sub>;

provided that no more than three of Xaa<sub>3</sub>, Xaa<sub>4</sub>, Xaa<sub>5</sub>, Xaa<sub>6</sub>, Xaa<sub>8</sub>, Xaa<sub>9</sub>, Xaa<sub>10</sub>, Xaa<sub>11</sub>,  
Xaa<sub>12</sub>, Xaa<sub>13</sub>, Xaa<sub>14</sub>, Xaa<sub>15</sub>, Xaa<sub>16</sub>, Xaa<sub>17</sub>, Xaa<sub>19</sub>, Xaa<sub>20</sub>, Xaa<sub>21</sub>, Xaa<sub>24</sub>, Xaa<sub>25</sub>, Xaa<sub>26</sub>, Xaa<sub>27</sub>  
and Xaa<sub>28</sub> are Ala; and provided also that, if Xaa<sub>1</sub> is His, Arg or Tyr, then at least one of  
Xaa<sub>3</sub>, Xaa<sub>4</sub> and Xaa<sub>9</sub> is Ala.